

L Number	Hits	Search Text	DB	Time stamp
1	23	hadlaczky\$.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/17 10:10

=> D L25 1-19 IBIB ABS

L25 ANSWER 1 OF 19 MEDLINE  
ACCESSION NUMBER: 2002008965 MEDLINE  
DOCUMENT NUMBER: 21237598 PubMed ID: 11338924  
TITLE: Satellite DNA-based artificial chromosomes for use in gene therapy.  
AUTHOR: Hadlaczky G  
CORPORATE SOURCE: Institute of Genetics, Biological Research Center,  
Hungarian Academy of Sciences, H-6701 Szeged, PO Box 521,  
Hungary.. hgy@nucleus.szbk.u-szeged.hu  
SOURCE: Curr Opin Mol Ther, (2001 Apr) 3 (2) 125-32. Ref: 33  
Journal code: 100891485. ISSN: 1464-8431.  
PUB. COUNTRY: England: United Kingdom  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200112  
ENTRY DATE: Entered STN: 20020121  
Last Updated on STN: 20020121  
Entered Medline: 20011205  
AB Satellite DNA-based artificial chromosomes (**SATACs**) can be made by induced de novo chromosome formation in cells of different mammalian species. These artificially generated accessory chromosomes are composed of predictable DNA sequences and they contain defined genetic information. Prototype human **SATACs** have been successfully constructed in different cell types from 'neutral' endogenous DNA sequences from the short arm of the human chromosome 15. **SATACs** have already passed a number of hurdles crucial to their further development as gene therapy vectors, including: large-scale purification; transfer of purified artificial chromosomes into different cells and embryos; generation of transgenic animals and germline transmission with purified **SATACs**; and the tissue-specific expression of a therapeutic gene from an artificial chromosome in the milk of transgenic animals.

L25 ANSWER 2 OF 19 MEDLINE  
ACCESSION NUMBER: 2000493348 MEDLINE  
DOCUMENT NUMBER: 20297740 PubMed ID: 10841045  
TITLE: Generation of transgenic mice and germline transmission of a mammalian artificial chromosome introduced into embryos by pronuclear microinjection.  
AUTHOR: Co D O; Borowski A H; Leung J D; van der Kaa J; Hengst S; Platenburg G J; Pieper F R; Perez C F; Jirik F R; Drayer J I  
CORPORATE SOURCE: Chromos Molecular Systems, Inc., Burnaby, British Columbia, Canada.. dco@chromos.com  
SOURCE: CHROMOSOME RESEARCH, (2000) 8 (3) 183-91.  
Journal code: 9313452. ISSN: 0967-3849.  
PUB. COUNTRY: Netherlands  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200010  
ENTRY DATE: Entered STN: 20001027  
Last Updated on STN: 20001027  
Entered Medline: 20001016

AB We have generated transgenic mice by pronuclear microinjection of a murine satellite DNA-based artificial chromosome (**SATAC**). As 50% of the founder progeny were **SATAC**-positive, this demonstrates that **SATAC** transmission through the germline had occurred. FISH analyses of metaphase chromosomes from mitogen-activated peripheral blood lymphocytes from both the founder and progeny revealed that the

**SATAC** was maintained as a discrete chromosome and that it had not integrated into an endogenous chromosome. To our knowledge, this is the first report of the germline transmission of a genetically engineered mammalian artificial chromosome within transgenic animals generated through pronuclear microinjection. We have also shown that murine **SATACs** can be similarly introduced into bovine embryos. The use of embryo microinjection to generate transgenic mammals carrying genetically engineered chromosomes provides a novel method by which the unique advantages of chromosome-based gene delivery systems can be exploited.

L25 ANSWER 3 OF 19 MEDLINE  
ACCESSION NUMBER: 2000019596 MEDLINE  
DOCUMENT NUMBER: 20019596 PubMed ID: 10554168  
TITLE: Mammalian artificial chromosome pilot production facility: large-scale isolation of functional satellite DNA-based artificial chromosomes.  
AUTHOR: deJong G; Telenius A H; Telenius H; Perez C F; Drayer J I; Hadlaczky G  
CORPORATE SOURCE: Chromos Molecular Systems, Inc., Vancouver, British Columbia, Canada.. gdejong@chromos.com  
SOURCE: CYTOMETRY, (1999 Feb 1) 35 (2) 129-33.  
Journal code: 8102328. ISSN: 0196-4763.  
PUB. COUNTRY: United States  
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)  
FILE SEGMENT: English  
ENTRY MONTH: Priority Journals  
199911  
ENTRY DATE: Entered STN: 20000113  
Last Updated on STN: 20000113  
Entered Medline: 19991130  
AB BACKGROUND: A pilot production facility has been established to isolate mammalian artificial chromosomes at high purity by using flow cytometric techniques. Dicentric chromosomes have been generated by the targeted amplification of pericentric heterochromatic and centromeric DNA by activating the "megareplicator." Breakage of these dicentric chromosomes generates satellite DNA-based artificial chromosomes (**SATAC**) from 60 to 400 megabases. METHODS: For large-scale production, we have developed cell lines capable of carrying one or two **SATACs**. A **SATAC**, because of a high adenine-thymine (AT) composition, is easily identified and sorted by using chromomycin A3 and Hoechst 33258 stains and a dual laser high-speed flow cytometer. A prototype **SATAC** (60 megabases) has been characterized. The prototype **SATAC** has been isolated from an original rodent/human hybrid cell line and transferred by using modified microcell fusion into a CHO production cell line. RESULTS: Metaphase chromosomes from this production cell line were isolated in a modified polyamine buffer, stained, and sorted by using a modified sheath buffer that maintains condensed chromosomes. **SATACs** are routinely sorted at rates greater than 1 million per hour. Sorted **SATACs** have been transferred to a variety of cells by using microcell fusion technology and were found to be functional. CONCLUSIONS: By developing new **SATAC** containing cell lines with fewer numbers of chromosomes in conjunction with operating a high speed flow sorter we have effectively generated an efficient production facility geared purely for the isolation of **SATACs**.

L25 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:336165 CAPLUS  
DOCUMENT NUMBER: 136:96714  
TITLE: Satellite DNA-based artificial chromosomes for use in gene therapy  
AUTHOR(S): Hadlaczky, Gyula  
CORPORATE SOURCE: Institute of Genetics Biological Research Center, Hungarian Academy of Sciences, Szeged, H-6701, Hung.  
SOURCE: Current Opinion in Molecular Therapeutics (2001),

3 (2), 125-132  
CODEN: CUOTFO; ISSN: 1464-8431  
PUBLISHER: PharmaPress Ltd.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English  
AB A review with refs. Satellite DNA-based artificial chromosomes (SATAcs) can be made by induced de novo chromosome formation in cells of different mammalian species. These artificially generated accessory chromosomes are composed of predictable DNA sequences and they contain defined genetic information. Prototype human SATAcs have been successfully constructed in different cell types from "neutral" endogenous DNA sequences from the short arm of the human chromosome 15. SATAcs have already passed a no. of hurdles crucial to their further development as gene therapy vectors, including: large-scale purifn.; transfer of purified artificial chromosomes into different cells and embryos; generation of transgenic animals and germline transmission with purified SATAcs; and the tissue-specific expression of a therapeutic gene from an artificial chromosome in the milk of transgenic animals.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:716318 CAPLUS  
DOCUMENT NUMBER: 134:232422  
TITLE: Satellite DNA-based artificial chromosomes-chromosomal vectors. Reply to Comments  
AUTHOR(S): Brown, William R. A.  
CORPORATE SOURCE: Institute of Genetics, University of Nottingham, Nottingham, UK  
SOURCE: Trends in Biotechnology (2000), 18(10), 403  
CODEN: TRBIDM; ISSN: 0167-7799  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB A polemic in response to Carl Perez et al. (ibid. 402-403). .

L25 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:716317 CAPLUS  
DOCUMENT NUMBER: 134:232421  
TITLE: Satellite DNA-based artificial chromosomes-chromosomal vectors. Comments  
AUTHOR(S): Perez, Carl; de Jong, Gary; Drayer, Jan  
CORPORATE SOURCE: Chromos Molecular Systems Inc., Burnaby, BC, Can.  
SOURCE: Trends in Biotechnology (2000), 18(10), 402-403  
CODEN: TRBIDM; ISSN: 0167-7799  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB A polemic in response to W.R.A. Brown et al. (ibid., 18(5), 218-223). Attention was brought to the existence of another chromosome-based vector technol. -- satellite DNA-based artificial chromosomes (SATAcs).

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:416625 CAPLUS  
DOCUMENT NUMBER: 133:39084  
TITLE: Artificial chromosomes, uses thereof and methods for preparing artificial chromosomes  
INVENTOR(S): Hadlaczky, Gyula; Szalay, Aladar A.  
PATENT ASSIGNEE(S): Chromos Molecular Systems, Inc., Can.; The Biological Research Center of the Hungarian Academy of Sciences  
SOURCE: U.S., 55 pp., Cont.-in-part of U. S. Ser. No. 629,822,

abandoned.  
CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6077697	A	20000620	US 1996-682080	19960715
US 6025155	A	20000215	US 1996-695191	19960807
CA 2250682	AA	19971030	CA 1997-2250682	19970410
WO 9740183	A2	19971030	WO 1997-US5911	19970410
WO 9740183	A3	19980205		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG		
AU 9724512	A1	19971112	AU 1997-24512	19970410
EP 929689	A2	19990721	EP 1997-920284	19970410
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI		
JP 2000508177	T2	20000704	JP 1997-538116	19970410
US 2001008025	A1	20010712	US 1998-96648	19980612
US 6228604	B1	20010508	US 1999-330317	19990610
			US 1996-629822	B2 19960410
			US 1996-682080	A2 19960715
			US 1996-695191	A 19960807
			WO 1997-US5911	W 19970410
			US 1998-99214P	P 19980904
			US 1998-152031	B2 19980911

PRIORITY APPLN. INFO.:

AB Methods for prep. cell lines that contain artificial chromosomes, methods for prepn. of artificial chromosomes, methods for purifn. of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes that, except for inserted heterologous DNA, are substantially composed of heterochromatin are provided. Methods for use of the artificial chromosomes, including for gene therapy, prodn. of gene products and prodn. of transgenic plants and animals are also provided. Methods for prep. cell lines that contain mammalian artificial chromosomes (MACs), methods for prepn. of artificial chromosomes, methods for purifn. of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes (**SATACs**) that, except for inserted heterologous DNA, are substantially composed of heterochromatin are provided; also provided are minichromosomes based on amplification of euchromatin. Methods for use of the artificial chromosomes, including for gene therapy, prodn. of gene products and prodn. of transgenic plants and animals are also provided.

REFERENCE COUNT: 297 THERE ARE 297 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DOCUMENT NUMBER: 133:276928  
 TITLE: Generation of transgenic mice and germline transmission of a mammalian artificial chromosome introduced into embryos by pronuclear microinjection  
 AUTHOR(S): Co, Deborah O.; Borowski, Anita H.; Leung, Josephine D.; Van der Kaa, Jos; Hengst, Sandra; Platenburg, Gerard J.; Pieper, Frank R.; Perez, Carl F.; Jirik, Frank R.; Drayer, Jan I.  
 CORPORATE SOURCE: Chromos Molecular Systems, Inc., Burnaby, BC, V5A 1W9, Can.  
 SOURCE: Chromosome Research (2000), 8(3), 183-191  
 CODEN: CRRSEE; ISSN: 0967-3849  
 PUBLISHER: Kluwer Academic Publishers  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB We have generated transgenic mice by pronuclear microinjection of a murine satellite DNA-based artificial chromosome (**SATAC**). As 50% of the founder progeny were **SATAC**-pos., this demonstrates that **SATAC** transmission through the germline had occurred. FISH analyses of metaphase chromosomes from mitogen-activated peripheral blood lymphocytes from both the founder and progeny revealed that the **SATAC** was maintained as a discrete chromosome and that it had not integrated into an endogenous chromosome. To our knowledge, this is the first report of the germline transmission of a genetically engineered mammalian artificial chromosome within transgenic animals generated through pronuclear microinjection. We have also shown that murine **SATACs** can be similarly introduced into bovine embryos. The use of embryo microinjection to generate transgenic mammals carrying genetically engineered chromosomes provides a novel method by which the unique advantages of chromosome-based gene delivery systems can be exploited.  
 REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:114388 CAPLUS  
 DOCUMENT NUMBER: 132:147617  
 TITLE: Artificial chromosomes, uses thereof and methods for preparing artificial chromosomes  
 INVENTOR(S): Hadlaczky, Gyula; Szalay, Aladar A.  
 PATENT ASSIGNEE(S): Chromos Molecular Systems, Inc., Can.; The Biological Research Center of the Hungarian Academy of Sciences  
 SOURCE: U.S., 59 pp., Cont.-in-part of U.S. Ser. No. 682,080.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6025155	A	20000215	US 1996-695191	19960807
US 6077697	A	20000620	US 1996-682080	19960715
CA 2250682	AA	19971030	CA 1997-2250682	19970410
WO 9740183	A2	19971030	WO 1997-US5911	19970410
WO 9740183	A3	19980205		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			

AU 9724512	A1	19971112	AU 1997-24512	19970410
EP 929689	A2	19990721	EP 1997-920284	19970410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9708855	A	20000104	BR 1997-8855	19970410
JP 2000508177	T2	20000704	JP 1997-538116	19970410
US 6228604	B1	20010508	US 1999-330317	19990610
PRIORITY APPLN. INFO.:				
			US 1996-629822	B2 19960410
			US 1996-682080	A2 19960715
			US 1996-682191	A 19960715
			US 1996-695191	A 19960807
			WO 1997-US5911	W 19970410
			US 1998-99214P	P 19980904
			US 1998-152031	B2 19980911

AB Methods for prep. cell lines that contain mammalian artificial chromosomes (MACs), methods for prepn. of artificial chromosomes, methods for purifn. of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes (**SATACs**) that, except for inserted heterologous DNA, are substantially composed of heterochromatin are provided; also provided are minichromosomes based on amplification of euchromatin. Methods for use of the artificial chromosomes, including for gene therapy, prodn. of gene products and prodn. of transgenic plants and animals are also provided.

REFERENCE COUNT: 318 THERE ARE 318 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:718036 CAPLUS  
 DOCUMENT NUMBER: 128:19355  
 TITLE: methods for prep. mammalian artificial chromosomes (MACs)  
 INVENTOR(S): Hadlaczky, Gyula; Szalay, Aladar A.  
 PATENT ASSIGNEE(S): Hadlaczky, Gyula, Hung.; Szalay, Aladar A.; American Gene Therapy, Inc.; Biological Research Center of the Hungarian Academy of Sciences; Loma Linda University  
 SOURCE: PCT Int. Appl., 248 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9740183	A2	19971030	WO 1997-US5911	19970410
WO 9740183	A3	19980205		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6077697	A	20000620	US 1996-682080	19960715
US 6025155	A	20000215	US 1996-695191	19960807
AU 9724512	A1	19971112	AU 1997-24512	19970410
EP 929689	A2	19990721	EP 1997-920284	19970410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

BR 9708855	A	20000104	BR 1997-8855	19970410
JP 2000508177	T2	20000704	JP 1997-538116	19970410
PRIORITY APPLN. INFO.:			US 1996-629822	A 19960410
			US 1996-682080	A 19960715
			US 1996-695191	A 19960807
			US 1996-682191	A 19960715
			WO 1997-US5911	W 19970410

AB Methods for prep. cell lines that contain artificial chromosomes, methods for prepn. of artificial chromosomes, methods for purifn. of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes [SATAcs] that, except for inserted heterologous DNA, are substantially composed of heterochromatin, are provided. Methods for use of the artificial chromosomes, including for gene therapy, prodn. of gene products and prodn. of transgenic plants and animals are also provided.

L25 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:625670 CAPLUS  
 DOCUMENT NUMBER: 123:37587  
 TITLE: Beneficiation of iron and manganese ores and recycling of metal bearing slags by means of air-pulsated BATAc jigs  
 AUTHOR(S): Wasmuth, Hans-Dieter; Ziaja, Dieter  
 CORPORATE SOURCE: Department Mineral Dressing Plants, KHD Humboldt Wedag AG, Cologne, Germany  
 SOURCE: Prog. Miner. Process. Technol., Proc. Int. Miner. Process. Symp., 5th (1994), 49-56. Editor(s): Demirel, Halim; Ersayin, Salih. Balkema: Rotterdam, Neth.  
 CODEN: 61LDAB  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

AB After minor modifications in design, the air pulsated BATAc jig a well known std. equipment for the prepn. of coal - can also be used for upgrading of intergrown hematite iron ores and manganese ores - lump ores as well as sinter fines, which require high sepn. densities to obtain marketable conc. grades. Furthermore the BATAc jig is also an appropriate unit for the recovery of the metal compds. of metal bearing slags. SATAc jigs are in com. operation in two big iron ore beneficiation plants in Australia and Brazil since many years. Furthermore, recently orders have been received for BATAc jigs to be used for beneficiation of manganese ores in Ghana and Namibia and recycling of ferrochromium slags in South Africa. The typical design of these BATAc jigs with their very sensitive stratification and discharge devices for efficient processing of ores and slags are described, and the particular flowsheets and design concepts of the new jigging plants are presented.

L25 ANSWER 12 OF 19 USPATFULL

ACCESSION NUMBER: 2001:110143 USPATFULL  
 TITLE: ARTIFICIAL CHROMOSOMES, USES THEREOF AND METHODS FOR PREPARING ARTIFICIAL CHROMOSOMES  
 INVENTOR(S): HADLACZKY, GYULA, SZAMOS, Hungary  
 SZALAY, ALADAR A., HIGHLAND, CA, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001008025	A1	20010712
APPLICATION INFO.:	US 1998-96648	A1	19980612 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1996-629822, filed on 10 Apr 1996, ABANDONED		
DOCUMENT TYPE:	Utility		

FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: STEPHANIE L. SEIDMAN, HELLER EHRMAN WHITE & MCAULIFFE,  
4250 EXECUTIVE SQUARE, 7TH FLOOR, LA JOLLA, CA,  
92037-9103  
NUMBER OF CLAIMS: 63  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 5 Drawing Page(s)  
LINE COUNT: 3855

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods for preparing cell lines that contain artificial chromosomes, methods for preparation of artificial chromosomes, methods for purification of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes that, except for inserted heterologous DNA, are substantially composed of heterochromatin are provided. Methods for use of the artificial chromosomes, including for gene therapy, production of gene products and production of transgenic plants and animals are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 13 OF 19 USPATFULL  
ACCESSION NUMBER: 2000:77213 USPATFULL  
TITLE: Artificial chromosomes, uses thereof and methods for preparing artificial chromosomes  
INVENTOR(S): Hadlaczky, Gyula, Szamos, Hungary  
Szalay, Aladar A., Highland, CA, United States  
PATENT ASSIGNEE(S): Chromos Molecular Systems, Inc., Canada (non-U.S. corporation)  
The Biological Research Center of the Hungarian Academy of Sciences, Hungary (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6077697		20000620
APPLICATION INFO.:	US 1996-682080		19960715 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1996-629822, filed on 10 Apr 1996, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Railey, II, Johnny F.		
LEGAL REPRESENTATIVE:	Seidman, Stephanie L. Heller, Ehrman, White & McAuliffe		
NUMBER OF CLAIMS:	64		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 5 Drawing Page(s)		
LINE COUNT:	4703		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods for preparing cell lines that contain artificial chromosomes, methods for preparation of artificial chromosomes, methods for purification of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes that, except for inserted heterologous DNA, are substantially composed of heterochromatin are provided. Methods for use of the artificial chromosomes, including for gene therapy, production of gene products and production of transgenic plants and animals are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 14 OF 19 USPATFULL  
 ACCESSION NUMBER: 2000:18241 USPATFULL  
 TITLE: Artificial chromosomes, uses thereof and methods for preparing artificial chromosomes  
 INVENTOR(S): Hadlaczky, Gyula, Szamos, Hungary  
 PATENT ASSIGNEE(S): Szalay, Aladar A., Highland, CA, United States  
 Chromos Molecular Systems, Inc., Canada (non-U.S. corporation)  
 The Biological Research Center of the Hungarian Academy of Sciences, Hungary (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6025155		20000215
APPLICATION INFO.:	US 1996-695191		19960807 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1996-682080, filed on 15 Jul 1996 which is a continuation-in-part of Ser. No. US 1996-629822, filed on 10 Apr 1996, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Railey, II, Johnny F.		
LEGAL REPRESENTATIVE:	Seidman, Stephanie L. Heller Ehrman White & McAuliffe		
NUMBER OF CLAIMS:	37		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 5 Drawing Page(s)		
LINE COUNT:	5465		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods for preparing cell lines that contain artificial chromosomes, methods for preparation of artificial chromosomes, methods for purification of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes that, except for inserted heterologous DNA, are substantially composed of heterochromatin are provided. Methods for use of the artificial chromosomes, including for gene therapy, production of gene products and production of transgenic plants and animals are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 15 OF 19 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 2001161268 EMBASE  
 TITLE: Satellite DNA-based artificial chromosomes for use in gene therapy.  
 AUTHOR: Hadlaczky G.  
 CORPORATE SOURCE: G. Hadlaczky, Institute of Genetics, Biological Research Center, Hungarian Academy of Sciences, PO Box 521, H-6701 Szeged, Hungary. hgy@nucleus.szbk.u-szeged.hu  
 SOURCE: Current Opinion in Molecular Therapeutics, (2001) 3/2 (125-132).  
 Refs: 33  
 ISSN: 1464-8431 CODEN: CUOTFO  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 022 Human Genetics  
 029 Clinical Biochemistry  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 AB Satellite DNA-based artificial chromosomes (**SATACs**) can be made by induced de novo chromosome formation in cells of different mammalian species. These artificially generated accessory chromosomes are composed

of predictable DNA sequences and they contain defined genetic information. Prototype human **SATACs** have been successfully constructed in different cell types from 'neutral' endogenous DNA sequences from the short arm of the human chromosome 15. **SATACs** have already passed a number of hurdles crucial to their further development as gene therapy vectors, including: large-scale purification; transfer of purified artificial chromosomes into different cells and embryos; generation of transgenic animals and germline transmission with purified **SATACs**; and the tissue-specific expression of a therapeutic gene from an artificial chromosome in the milk of transgenic animals.

L25 ANSWER 16 OF 19 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000171063 EMBASE

TITLE: Generation of transgenic mice and germline transmission of a mammalian artificial chromosome introduced into embryos by pronuclear microinjection.

AUTHOR: Co D.O.; Borowski A.H.; Leung J.D.; Van der Kaa J.; Hengst S.; Platenburg G.J.; Pieper F.R.; Perez C.F.; Jirik F.R.; Drayer J.I.

CORPORATE SOURCE: D.O. Co, Chromos Molecular Systems, Inc., 8081 Loughheed Highway, Burnaby, BC V5A 1W9, Canada. dco@chromos.com

SOURCE: Chromosome Research, (2000) 8/3 (183-191).  
Refs: 35

ISSN: 0967-3849 CODEN: CRRSEE

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics  
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB We have generated transgenic mice by pronuclear microinjection of a murine satellite DNA-based artificial chromosome (**SATAC**). As 50% of the founder progeny were **SATAC**-positive, this demonstrates that **SATAC** transmission through the germline had occurred. FISH analyses of metaphase chromosomes from mitogen-activated peripheral blood lymphocytes from both the founder and progeny revealed that the **SATAC** was maintained as a discrete chromosome and that it had not integrated into an endogenous chromosome. To our knowledge, this is the first report of the germline transmission of a genetically engineered mammalian artificial chromosome within transgenic animals generated through pronuclear microinjection. We have also shown that murine **SATACs** can be similarly introduced into bovine embryos. The use of embryo microinjection to generate transgenic mammals carrying genetically engineered chromosomes provides a novel method by which the unique advantages of chromosome-based gene delivery systems can be exploited.

L25 ANSWER 17 OF 19 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999041146 EMBASE

TITLE: Mammalian artificial chromosome pilot production facility: Large-scale isolation of functional satellite DNA-based artificial chromosomes.

AUTHOR: deJong G.; Telenius A.H.; Telenius H.; Perez C.F.; Drayer J.I.; Hadlaczky G.

CORPORATE SOURCE: G. deJong, Chromos Molecular Systems, Inc., 6660 Northwest Marine Drive, Vancouver, BC V6T 1Z4, Canada.  
gdejong@chromos.com

SOURCE: Cytometry, (1 Feb 1999) 35/2 (129-133).  
Refs: 12

ISSN: 0196-4763 CODEN: CYTODQ

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 021 Developmental Biology and Teratology  
022 Human Genetics  
029 Clinical Biochemistry

LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Background: A pilot production facility has been established to isolate mammalian artificial chromosomes at high purity by using flow cytometric techniques. Dicentric chromosomes have been generated by the targeted amplification of pericentric heterochromatic and centromeric DNA by activating the 'megareplicator.' Breakage of these dicentric chromosomes generates satellite DNA-based artificial chromosomes (**SATAC**) from 60 to 400 megabases. Methods: For large-scale production, we have developed cell lines capable of carrying one or two **SATACs**. A **SATAC**, because of a high adenine-thymine (AT) composition, is easily identified and sorted by using chromomycin A3 and Hoechst 33258 stains and a dual laser high-speed flow cytometer. A prototype **SATAC** (60 megabases) has been characterized. The prototype **SATAC** has been isolated from an original rodent/human hybrid cell line and transferred by using modified microcell fusion into a CHO production cell line. Results: Metaphase chromosomes from this production cell line were isolated in a modified polyamine buffer, stained, and sorted by using a modified sheath buffer that maintains condensed chromosomes. **SATACs** are routinely sorted at rates greater than 1 million per hour. Sorted **SATACs** have been transferred to a variety of cells by using microcell fusion technology and were found to be functional. Conclusions: By developing new **SATAC** containing cell lines with fewer numbers of chromosomes in conjunction with operating a high speed flow sorter we have effectively generated an efficient production facility geared purely for the isolation of **SATACs**.

L25 ANSWER 18 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:324274 BIOSIS  
DOCUMENT NUMBER: PREV200000324274  
TITLE: Generation of transgenic mice and germline transmission of a mammalian artificial chromosome introduced into embryos by pronuclear microinjection.  
AUTHOR(S): Co, Deborah O. (1); Borowski, Anita H.; Leung, Josephine D. (1); van der Kaa, Jos; Hengst, Sandra; Platenburg, Gerard J.; Pieper, Frank R.; Perez, Carl F. (1); Jirik, Frank R.; Drayer, Jan I. (1)  
CORPORATE SOURCE: (1) Chromos Molecular Systems, Inc., 8081 Lougheed Highway, Burnaby, British Columbia, V5A 1W9 Canada  
SOURCE: Chromosome Research, (2000) Vol. 8, No. 3, pp. 183-191.  
print.  
ISSN: 0967-3849.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB We have generated transgenic mice by pronuclear microinjection of a murine satellite DNA-based artificial chromosome (**SATAC**). As 50% of the founder progeny were **SATAC**-positive, this demonstrates that **SATAC** transmission through the germline had occurred. FISH analyses of metaphase chromosomes from mitogen-activated peripheral blood lymphocytes from both the founder and progeny revealed that the **SATAC** was maintained as a discrete chromosome and that it had not integrated into an endogenous chromosome. To our knowledge, this is the first report of the germline transmission of a genetically engineered mammalian artificial chromosome within transgenic animals generated through pronuclear microinjection. We have also shown that murine **SATACs** can be similarly introduced into bovine embryos. The use of embryo microinjection to generate transgenic mammals carrying genetically engineered chromosomes provides a novel method by which the unique advantages of chromosome-based gene delivery systems can be exploited.

L25 ANSWER 19 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1999:104500 BIOSIS  
DOCUMENT NUMBER: PREV199900104500

TITLE: Mammalian artificial chromosome pilot production facility:  
Large-scale isolation of functional satellite DNA-based  
artificial chromosomes.

AUTHOR(S): DeJong, Gary (1); Telenius, Adele H.; Telenius, Hakan;  
Perez, Carl F.; Drayer, Jan I.; Hadlaczky, Gyula

Corporate Source: (1) Chromos Mol. Syst. Inc., 6660 Northwest Marine Drive,  
Vancouver, BC V6T 1Z4 Canada

SOURCE: Cytometry, (Feb. 1, 1999) Vol. 35, No. 2, pp. 129-133.  
ISSN: 0196-4763.

DOCUMENT TYPE: Article  
LANGUAGE: English

AB Background: A pilot production facility has been established to isolate mammalian artificial chromosomes at high purity by using flow cytometric techniques. Dicentric chromosomes have been generated by the targeted amplification of pericentric heterochromatic and centromeric DNA by activating the "megareplicator." Breakage of these dicentric chromosomes generates satellite DNA-based artificial chromosomes (**SATAC**) from 60 to 400 megabases. Methods: For large-scale production, we have developed cell lines capable of carrying one or two **SATACs**. A **SATAC**, because of a high adenine-thymine (A:T) composition, is easily identified and sorted by using chromomycin A3 and Hoechst 33258 stains and a dual laser high-speed flow cytometer. A prototype **SATAC** (60 megabases) has been characterized. The prototype **SATAC** has been isolated from an original rodent/human hybrid cell line and transferred by using modified microcell fusion into a CHO production cell line. Results: Metaphase chromosomes from this production cell line were isolated in a modified polyamine buffer, stained, and sorted by using a modified sheath buffer that maintains condensed chromosomes. **SATACs** are routinely sorted at rates greater than 1 million per hour. Sorted **SATACs** have been transferred to a variety of cells by using microcell fusion technology and were found to be functional. Conclusions: By developing new **SATAC** containing cell lines with fewer numbers of chromosomes in conjunction with operating a high speed flow sorter we have effectively generated an efficient production facility geared purely for the isolation of **SATACs**.

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3 ANSWER 10 OF 11      MEDLINE      DUPLICATE 9

ACCESSION NUMBER: 83180419      MEDLINE

DOCUMENT NUMBER: 83180419      PubMed ID: 6301685

TITLE: Amplification of rDNA and type I sequences in Drosophila males deficient in rDNA.

AUTHOR: de Cicco D V; Glover D M

SOURCE: CELL, (1983 Apr) 32 (4) 1217-25.  
Journal code: 0413066. ISSN: 0092-8674.

PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198306

ENTRY DATE: Entered STN: 19900318  
Last Updated on STN: 19990129  
Entered Medline: 19830617

AB rDNA magnification is a heritable change in rDNA content that occurs in *D. melanogaster* males when chromosomes deficient in rDNA are placed together for several generations. We have examined the restriction endonuclease cleavage pattern of the rDNA from an X chromosome undergoing magnification, and find no evidence for the selective amplification of either uninterrupted rDNA units or those containing insertion sequences. In addition, we observe an amplification of rDNA in the first generation of extremely bobbed male progeny to a level exceeding that of wild-type flies, but that reduces to the wild-type level in subsequent generations. The type I rDNA insertion elements also occur as tandem arrays, independently of rDNA. Southern hybridizations indicate that the majority of these sequences are located in the **heterochromatin** surrounding the nucleolus organizer on the X chromosome, and we find that they, too, **amplify** transiently in the first generation of magnifying males.

L48 ANSWER 1 OF 2 MEDLINE  
 ACCESSION NUMBER: 2001038301 MEDLINE  
 DOCUMENT NUMBER: 20411244 PubMed ID: 10954419  
 TITLE: Novel generation of human satellite DNA-based artificial chromosomes in mammalian cells.  
 AUTHOR: Csonka E; Cserpan I; Fodor K; Hollo G; Katona R; Kereso J; Praznovszky T; Szakal B; Telenius A; deJong G; Udvardy A; Hadlaczky G  
 CORPORATE SOURCE: Institute of Genetics, Biological Research Center, Hungarian Academy of Sciences, H-6701 Szeged, PO Box 521, Hungary.  
 SOURCE: JOURNAL OF CELL SCIENCE, (2000 Sep) 113 ( Pt 18) 3207-16.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200011  
 ENTRY DATE: Entered STN: 20010322  
                   Last Updated on STN: 20010322  
                   Entered Medline: 20001129

**AB** An in vivo approach has been developed for generation of artificial chromosomes, based on the induction of intrinsic, large-scale amplification mechanisms of mammalian cells. Here, we describe the successful generation of prototype human satellite DNA-based artificial chromosomes via amplification-dependent de novo chromosome formations induced by integration of exogenous DNA sequences into the centromeric/rDNA regions of human acrocentric chromosomes. Subclones with mitotically stable de novo chromosomes were established, which allowed the initial characterization and purification of these artificial chromosomes. Because of the low complexity of their DNA content, they may serve as a useful tool to study the structure and function of higher eukaryotic chromosomes. Human satellite DNA-based artificial chromosomes containing amplified satellite DNA, rDNA, and exogenous DNA sequences were heterochromatic, however, they provided a suitable chromosomal environment for the expression of the integrated exogenous genetic material. We demonstrate that induced de novo chromosome formation is a reproducible and effective methodology in generating artificial chromosomes from predictable sequences of different mammalian species. Satellite DNA-based artificial chromosomes formed by induced large-scale amplifications on the short arm of human acrocentric chromosomes may become safe or low risk vectors in gene therapy.

L48 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:718036 CAPLUS  
 DOCUMENT NUMBER: 128:19355  
 TITLE: methods for prep. mammalian artificial chromosomes (MACs)  
 INVENTOR(S): Hadlaczky, Gyula; Szalay, Aladar A.  
 PATENT ASSIGNEE(S): Hadlaczky, Gyula, Hung.; Szalay, Aladar A.; American Gene Therapy, Inc.; Biological Research Center of the Hungarian Academy of Sciences; Loma Linda University  
 SOURCE: PCT Int. Appl., 248 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9740183	A2	19971030	WO 1997-US5911	19970410
WO 9740183	A3	19980205		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,  
 DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,  
 LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,  
 PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ,  
 VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,  
 GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,  
 ML, MR, NE, SN, TD, TG  
 US 6077697 A 20000620 US 1996-682080 19960715  
 US 6025155 A 20000215 US 1996-695191 19960807  
 AU 9724512 A1 19971112 AU 1997-24512 19970410  
 EP 929689 A2 19990721 EP 1997-920284 19970410  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI  
 BR 9708855 A 20000104 BR 1997-8855 19970410  
 JP 2000508177 T2 20000704 JP 1997-538116 19970410  
 PRIORITY APPLN. INFO.: US 1996-629822 A 19960410  
 US 1996-682080 A 19960715  
 US 1996-695191 A 19960807  
 US 1996-682191 A 19960715  
 WO 1997-US5911 W 19970410  
**AB** Methods for prep. cell lines that contain artificial chromosomes, methods for prepn. of artificial chromosomes, methods for purifn. of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes [SATACs] that, except for inserted heterologous DNA, are substantially composed of heterochromatin, are provided. Methods for use of the artificial chromosomes, including for gene therapy, prodn. of gene products and prodn. of transgenic plants and animals are also provided.

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L46 ANSWER 13 OF 15 USPATFULL

DUPLICATE 13

ACCESSION NUMBER: 94:15649 USPATFULL  
TITLE: Mammalian artificial chromosomes  
INVENTOR(S): Hadlaczky, Gyula, Szamos, Hungary  
PATENT ASSIGNEE(S): Biologic Research Center of the Hungarian Academy of Sciences, Hungary (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5288625		19940222
APPLICATION INFO.:	US 1991-759558		19910913 (7)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Schwartz, Richard A.		
ASSISTANT EXAMINER:	Ketter, James		
LEGAL REPRESENTATIVE:	Banner, Birch, McKie & Beckett		
NUMBER OF CLAIMS:	12		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	17 Drawing Figure(s); 3 Drawing Page(s)		
LINE COUNT:	499		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Non-human cell lines are disclosed which contain functional centromeres comprising human DNA sequences linked to a dominant marker gene. The centromeres are carried on stable chromosomes which carry no centromeres other than those comprising human DNA sequences. The cell lines can be used to isolate the chromosomes as well as for use in inserting genes into mammalian cells. Methods are taught for generating such cell lines from cell lines carrying dicentric chromosomes.

L46 ANSWER 11 OF 15 MEDLINE DUPLICATE 11  
ACCESSION NUMBER: 96385350 MEDLINE  
DOCUMENT NUMBER: 96385350 PubMed ID: 8793208  
TITLE: De novo chromosome formations by large-scale amplification  
of the centromeric region of mouse chromosomes.  
AUTHOR: Kereso J; Praznovszky T; Cserpan I; Fodor K; Katona R;  
Csonka E; Fattyol K; Hollo G; Szeles A; Ross A R; Sumner A  
T; Szalay A A; Hadlaczky G  
CORPORATE SOURCE: Institute of Genetics, Hungarian Academy of Sciences,  
Szeged, Hungary.  
SOURCE: CHROMOSOME RESEARCH, (1996 Apr) 4 (3) 226-39.  
Journal code: 9313452. ISSN: 0967-3849.  
PUB. COUNTRY: ENGLAND: United Kingdom  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199612  
ENTRY DATE: Entered STN: 19970128  
Last Updated on STN: 19970128  
Entered Medline: 19961209

AB Chromosomes formed de novo which originated from the centromeric region of mouse chromosome 7, have been analysed. These new chromosomes were formed by apparently similar large-scale amplification processes, and are organized into amplicons of approximately 30 Mb. Centromeric satellite DNA was found to be the constant component of all amplicons. Satellite DNA sequences either bordered the large euchromatic amplicons (E-type amplification), or made up the bulk of the constitutive heterochromatic amplicons (H-type amplification). Detailed analysis of a heterochromatic megachromosome formed de novo by an H-type amplification revealed that it is composed of a tandem array of 10-12 large (approximately 30 Mb) amplicons each marked with integrated "foreign" DNA sequences at both ends. Each amplicon is a giant palindrome, consisting of two inverted doublets of approximately 7.5-Mb blocks of satellite DNA. Our results indicate that the building units of the **pericentric** heterochromatin of mouse chromosomes are approximately 7.5-Mb blocks of satellite DNA flanked by non-satellite sequences. We suggest that the formation de novo of various chromosome segments and chromosomes seen in different cell lines may be the result of large-scale E- and H-type amplification initiated in the **pericentric** region of chromosomes.

L46 ANSWER 10 OF 15 MEDLINE DUPLICATE 10  
ACCESSION NUMBER: 96385351 MEDLINE  
DOCUMENT NUMBER: 96385351 PubMed ID: 8793209  
TITLE: Evidence for a megareplicon covering megabases of centromeric chromosome segments.  
AUTHOR: Hollo G; Kereso J; Praznovszky T; Cserpan I; Fodor K; Katona R; Csonka E; Fatyol K; Szeles A; Szalay A A; Hadlaczky G  
CORPORATE SOURCE: Institute of Genetics, Hungarian Academy of Sciences, Szeged, Hungary.  
SOURCE: CHROMOSOME RESEARCH, (1996 Apr) 4 (3) 240-7.  
Journal code: 9313452. ISSN: 0967-3849.  
PUB. COUNTRY: ENGLAND: United Kingdom  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199612  
ENTRY DATE: Entered STN: 19970128  
Last Updated on STN: 19970128  
Entered Medline: 19961209

AB We have analysed the replication of the heterochromatic megachromosome that was formed de novo by a large-scale amplification process initiated in the centromeric region of mouse chromosome 7. The megachromosome is organized into amplicons approximately 30 Mb in size, and each amplicon consists of two large inverted repeats delimited by a primary replication initiation site. Our results suggest that these segments represent a higher order replication unit (megareplicon) of the centromeric region of mouse chromosomes. Analysis of the replication of the megareplicons indicates that the **pericentric** heterochromatin and the centromere of mouse chromosomes begin to replicate early, and that their replication continues through approximately three-quarters of the S-phase. We suggest that a replication-directed mechanism may account for the initiation of large-scale amplification in the centromeric regions of mouse chromosomes, and may also explain the formation of new, stable chromosome segments and chromosomes.